

CLAIMS

What is claimed:

1. A method for expansion of a stem cell comprising contacting the stem cell in vitro with an amount of a modulator of an AML1-ETO target factor function effective to inhibit differentiation of the stem cell while not inhibiting self-renewal of the stem cell, and exposing the stem cell to cell growth conditions such that the cell proliferates.
2. The method of claim 1 wherein the cell is a hematopoietic stem cell.
3. The method of claim 2 where the hematopoietic stem cells are isolated from bone marrow, cord blood, peripheral blood CD34+ cell populations or peripheral blood CD34- cell populations.
4. The method of claim 2 where the hematopoietic stem cells are derived from a human.
5. The method of claim 1 where the expansion is carried out in vitro.
6. The method of claim 1 where the stem cells are isolated from a tissue selected from the group consisting of pancreas, muscle, nerve, skin and adipose.
7. The method of claim of claim 1 where the stem cell is purified or partially purified.
8. The method of claim 1 where the expansion is carried out in vivo.
9. The method of claim 1 where the AML1-ETO target factor is a transcription factor.
10. The method of claim 9 where the transcription factor is selected from the group consisting of AML1, C/EBP alpha, PU.1 and a combination of any of the foregoing.
11. The method of claim 1 where the modulation of an AML1-ETO target factor function is an inhibition of function.
12. The method of claim 1 where the modulation of an AML1-ETO target factor function is a stimulation of function.
13. The method of claim 1 where the modulation of an AML1-ETO target factor function is a translocation of function.
14. The method of claim 11 where the inhibition occurs as a result of inhibition of the synthesis of the AML1-ETO target factor.
15. The method of claim 14 where the inhibition is a total inhibition or a partial inhibition.
16. The method of claim 14 where the AML1-ETO target factor is selected from the group consisting of AML1, C/EBP alpha, PU.1 and a combination of any of the foregoing.
17. The method of claim 11 where the inhibition occurs as a result of inhibition of interaction with cellular factors that contributes to the activity of the AML1-ETO target factor.

18. The method of claim 17 where the inhibition is a total inhibition or a partial inhibition.
19. The method of claim 17 where the AML1-ETO target factor is selected from the group consisting of AML1, C/EBP alpha, PU.1 and a combination of any of the foregoing.
20. The method of claim 11 where the inhibition occurs as a result of inhibition of DNA binding of the AML1-ETO target factor.
21. The method of claim 20 where the inhibition is a total inhibition or a partial inhibition.
22. The method of claim 20 where the AML1-ETO target factor is selected from the group consisting of AML1, C/EBP alpha, PU.1 and a combination of any of the foregoing.
23. The method of claim 11 where the inhibition occurs as a result of stimulated degradation of mRNA encoding the AML1-ETO target factor.
24. The method of claim 23 where the inhibition is a total inhibition or a partial inhibition.
25. The method of claim 23 where the AML1-ETO target factor is selected from the group consisting of AML1, C/EBP alpha, PU.1 and a combination of any of the foregoing.
26. The method of claim 11 where the inhibition occurs as a result of inhibition of transcription of the AML1-ETO target factor.
27. The method of claim 26 where the inhibition is a total inhibition or a partial inhibition.
28. The method of claim 26 where the AML1-ETO target factor is selected from the group consisting of AML1, C/EBP alpha, PU.1 and a combination of any of the foregoing.
29. The method of claim 26 where said inhibition of transcription is accomplished using small interfering RNAs.
30. The method of claim 1 where the modulator of an AML1-ETO target factor function is an AML1-ETO fusion protein.
31. The method of claim 30 where said AML1-ETO fusion protein is expressed in said stem cell.
32. The method of claim 31 where said expression is a transient expression.
33. The method of claim 30 where said AML1-ETO fusion protein comprises a domain that reversibly activates and inactivates an AML1-ETO fusion protein function in the presence and absence, respectively, of an inducer.
34. The method of claim 33 where the domain is the hormone binding domain of the estrogen receptor and the inducer is estrogen or tamoxifen.
35. The method of claim 1 where the modulator of an AML1-ETO target factor function is an inhibitor of an AML1 activity.
36. The method of claim 1 where the modulator of an AML1-ETO target factor function is an inhibitor of a C/EBP alpha activity.
37. The method of claim 1 where the modulator of an AML1-ETO target factor function is an inhibitor of a PU.1 activity.

38. The method according to claim 1 wherein said contacting is carried out by culturing said precursor cell in medium containing a purified agonist in soluble form.
39. The method according to claim 1 wherein substantially no differentiation of the cell occurs.
40. The method of claim 1 where said modulating is direct or indirect.
41. A method to inhibit the differentiation and to promote the self renewal of mammalian stem cells by modulating a function of an AML1-ETO target factor.
42. The method of claim 41 wherein the mammalian stem cell is a hematopoietic stem cell.
43. The method of claim 42 where the hematopoietic stem cells are isolated from bone marrow, cord blood, peripheral blood CD34+ cell populations or peripheral blood CD34- cell populations.
44. The method of claim 42 where the hematopoietic stem cells are derived from a human.
45. The method of claim 42 where the expansion is carried out in vitro.
46. The method of claim 41 where the stem cells are isolated from a tissue selected from the group consisting of pancreas, muscle, nerve, skin and adipose.
47. The method of claim of claim 41 where the stem cell is purified or partially purified.
48. The method of claim 41 where the expansion is carried out in vivo.
49. The method of claim 41 where the AML1-ETO target factor is a transcription factor.
50. The method of claim 49 where the transcription factor is selected from the group consisting of AML1, C/EBP alpha, PU.1 and a combination of any of the foregoing.
51. The method of claim 41 where the modulation of an AML1-ETO target factor function is an inhibition of function.
52. The method of claim 41 where the modulation of an AML1-ETO target factor function is a stimulation of function.
53. The method of claim 41 where the modulation of an AML1-ETO target factor function is a translocation of function.
54. The method of claim 41 where the inhibition occurs as a result of inhibition of the synthesis of the AML1-ETO target factor.
55. The method of claim 54 where the inhibition is a total inhibition or a partial inhibition.
56. The method of claim 54 where the AML1-ETO target factor is selected from the group consisting of AML1, C/EBP alpha, PU.1 and a combination of any of the foregoing.
57. The method of claim 41 where the inhibition occurs as a result of inhibition of interaction with cellular factors that contributes to the activity of the AML1-ETO target factor.
58. The method of claim 57 where the inhibition is a total inhibition or a partial inhibition.
59. The method of claim 57 where the AML1-ETO target factor is selected from the group consisting of AML1, C/EBP alpha, PU.1 and a combination of any of the foregoing.

60. The method of claim 41 where the inhibition occurs as a result of inhibition of DNA binding of the AML1-ETO target factor.
61. The method of claim 60 where the inhibition is a total inhibition or a partial inhibition.
62. The method of claim 60 where the AML1-ETO target factor is selected from the group consisting of AML1, C/EBP alpha, PU.1 and a combination of any of the foregoing.
63. The method of claim 41 where the inhibition occurs as a result of stimulated degradation of mRNA encoding the AML1-ETO target factor.
64. The method of claim 63 where the inhibition is a total inhibition or a partial inhibition.
65. The method of claim 63 where the AML1-ETO target factor is selected from the group consisting of AML1, C/EBP alpha, PU.1 and a combination of any of the foregoing.
66. The method of claim 41 where the inhibition occurs as a result of inhibition of transcription of the AML1-ETO target factor.
67. The method of claim 66 where the inhibition is a total inhibition or a partial inhibition.
68. The method of claim 66 where the AML1-ETO target factor is selected from the group consisting of AML1, C/EBP alpha, PU.1 and a combination of any of the foregoing.
69. The method of claim 66 where said inhibition of transcription is accomplished using small interfering RNAs.
70. The method of claim 41 where the modulator of an AML1-ETO target factor function is an AML1-ETO fusion protein.
71. The method of claim 70 where said AML1-ETO fusion protein is expressed in said stem cell.
72. The method of claim 71 where said expression is a transient expression.
73. The method of claim 70 where said AML1-ETO fusion protein comprises a domain that reversibly activates and inactivates an AML1-ETO fusion protein function in the presence and absence, respectively, of an inducer.
74. The method of claim 73 where the domain is the hormone binding domain of the estrogen receptor and the inducer is estrogen or tamoxifen.
75. The method of claim 41 where the modulator of an AML1-ETO target factor function is an inhibitor of an AML1 activity.
76. The method of claim 41 where the modulator of an AML1-ETO target factor function is an inhibitor of a C/EBP alpha activity.
77. The method of claim 41 where the modulator of an AML1-ETO target factor function is an inhibitor of a PU.1 activity.
78. The method according to claim 41 wherein said contacting is carried out by culturing said precursor cell in medium containing a purified agonist in soluble form.
79. The method according to claim 41 wherein substantially no differentiation of the cell occurs.

80. The method of claim 41 where said modulation is direct or indirect.
81. A method for cell transplantation comprising contacting a mammalian stem cell in vitro with an amount of a modulator of an AML1-ETO target factor function effective to inhibit differentiation of the cell while not inhibiting self-renewal of the cell, exposing the cell in vitro to cell growth conditions to create an expanded stem cell population and administering an amount of the expanded stem cell population or progeny cells thereof to a patient in need of such transplantation.
82. The method claim 81 wherein the patient is immunocompromised, immunosuppressed or immune deficient.
83. The method of claim 81 where the administration is intravenous administration.
84. The method of claim 81 wherein the mammalian stem cell is a hematopoietic stem cell.
85. The method of claim 84 where the hematopoietic stem cells are isolated from bone marrow, cord blood, peripheral blood CD34+ cell populations or peripheral blood CD34- cell populations.
86. The method of claim 84 where the hematopoietic stem cells are derived from a human.
87. The method of claim 84 where the expansion is carried out in vitro
88. The method of claim 81 where the stem cells are isolated from a tissue selected from the group consisting of pancreas, muscle, nerve, skin and adipose.
89. The method of claim of claim 81 where the stem cell is purified or partially purified.
90. The method of claim 81 where the expansion is carried out in vivo.
91. The method of claim 81 where the AML1-ETO target factor is a transcription factor.
92. The method of claim 91 where the transcription factor is selected from the group consisting of AML1, C/EBP alpha, PU.1 and a combination of any of the foregoing.
93. The method of claim 81 where the modulation of an AML1-ETO target factor function is an inhibition of function.
94. The method of claim 81 where the modulation of an AML1-ETO target factor function is a stimulation of function.
95. The method of claim 81 where the modulation of an AML1-ETO target factor function is a translocation of function.
96. The method of claim 93 where the inhibition occurs as a result of inhibition of the synthesis of the AML1-ETO target factor.
97. The method of claim 96 where the inhibition is a total inhibition or a partial inhibition.
98. The method of claim 96 where the AML1-ETO target factor is selected from the group consisting of AML1, C/EBP alpha, PU.1 and a combination of any of the foregoing.

99. The method of claim 93 where the inhibition occurs as a result of inhibition of interaction with cellular factors that contributes to the activity of the AML1-ETO target factor.
100. The method of claim 99 where the inhibition is a total inhibition or a partial inhibition.
101. The method of claim 99 where the AML1-ETO target factor is selected from the group consisting of AML1, C/EBP alpha, PU.1 and a combination of any of the foregoing.
102. The method of claim 93 where the inhibition occurs as a result of inhibition of DNA binding of the AML1-ETO target factor.
103. The method of claim 102 where the inhibition is a total inhibition or a partial inhibition.
104. The method of claim 102 where the AML1-ETO target factor is selected from the group consisting of AML1, C/EBP alpha, PU.1 and a combination of any of the foregoing.
105. The method of claim 93 where the inhibition occurs as a result of stimulated degradation of mRNA encoding the AML1-ETO target factor.
106. The method of claim 105 where the inhibition is a total inhibition or a partial inhibition.
107. The method of claim 105 where the AML1-ETO target factor is selected from the group consisting of AML1, C/EBP alpha, PU.1 and a combination of any of the foregoing.
108. The method of claim 93 where the inhibition occurs as a result of inhibition of transcription of the AML1-ETO target factor.
109. The method of claim 108 where the inhibition is a total inhibition or a partial inhibition.
110. The method of claim 108 where the AML1-ETO target factor is selected from the group consisting of AML1, C/EBP alpha, PU.1 and a combination of any of the foregoing.
111. The method of claim 108 where said inhibition of transcription is accomplished using small interfering RNAs.
112. The method of claim 81 where the modulator of an AML1-ETO target factor function is an AML1-ETO fusion protein.
113. The method of claim 112 where said AML1-ETO fusion protein is expressed in said stem cell.
114. The method of claim 113 where said expression is a transient expression.
115. The method of claim 112 where said AML1-ETO fusion protein comprises a domain that reversibly activates and inactivates an AML1-ETO fusion protein function in the presence and absence, respectively, of an inducer.
116. The method of claim 115 where the domain is the hormone binding domain of the estrogen receptor and the inducer is estrogen or tamoxifen.
117. The method of claim 81 where the modulator of an AML1-ETO target factor function is an inhibitor of an AML1 activity.

118. The method of claim 81 where the modulator of an AML1-ETO target factor function is an inhibitor of a C/EBP alpha activity.
119. The method of claim 81 where the modulator of an AML1-ETO target factor function is an inhibitor of a PU.1 activity.
120. The method according to claim 81 wherein said contacting is carried out by culturing said precursor cell in medium containing a purified agonist in soluble form.
121. The method according to claim 81 wherein substantially no differentiation of the cell occurs.
122. The method of claim 81 where said modulation is direct or indirect.
123. The method of claim 81 where the stem cells are selected from the group consisting of autologous, allogeneic and xenogenic.